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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/709,829	11/10/2000	James J. Fort	6488.US.02	3590

7590 02/20/2002

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EXAMINER
RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 02/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/709,829	Applicant(s) FORT ET AL.	
	Examiner Jeffrey E. Russel	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. The claim for priority under 35 U.S.C. 119(e) set forth at page 1, lines 2-4, of the specification is objected to because the serial number of the parent provisional application is incorrect. The correct series code for the parent provisional application is 60, not 06. Correction is required.

2. Claims 3-5 and 12-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 3 is indefinite because it is not clear when the protease inhibitor is supposed to be dissolved in an organic solvent, e.g., as part of the final pharmaceutical composition, or during a processing step by which the final pharmaceutical composition is formed. At claim 5, page 24, line 2, "or" should be changed to "and" so that standard Markush terminology is used. Claim 12, step (e), recites optionally grinding and sieving "the solid dispersion", but none of the previous steps recite that a solid dispersion has been formed. Accordingly, it is not clear what product of which step or steps may optionally be ground and sieved. For analogous reasons, it is not clear what product of which step or steps may be encapsulated or compressed into a tablet as recited in instant claims 13 and 14. Further with respect to claims 13 and 14, because claim 12, step (e), recites optionally grinding and sieving the solid dispersion to obtain a resultant product, it is not clear if claims 13 and 14 require encapsulating or compressing the solid dispersion without any grinding or sieving, or if claims 13 and 14 would embrace encapsulating or compressing the resultant product of claim 12, step (e).

3. Claims 5, 6, 8, 15, 20, and 21 are objected to because of the following informalities: At claim 5, line 4, a beginning parenthesis is missing from before "2S". In the chemical name of

ritonavir recited in claim 5, one of the beginning parentheses at claim 5, line 4, is unmatched. This same error occurs in the chemical name of ritonavir recited in claims 6, 8, 15, 20, and 21. At claim 5, page 23, line 19, the end parenthesis occurring after "2S*]" is unmatched. Appropriate correction is required.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not

only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

5. Claims 1-5 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by the Aungst et al article (Int. J. Pharmaceutics, Vol. 156, pages 79-88). The Aungst et al article teaches a solid dispersion of DMP 323, an HIV protease inhibitor, in PEG or PEG PVP matrices. A surfactant can also be present. See, e.g., the Abstract and Table 2. With respect to instant claims 3 and 4, note that method of making steps do not impart patentability to product claims which are otherwise anticipated by or obvious over the prior art.

6. Claim 19 is rejected under 35 U.S.C. 103(a) as being obvious over the Aungst et al article (Int. J. Pharmaceutics, Vol. 156, pages 79-88). Application of the Aungst et al article is the same as in the above rejection of claims 1-5 and 11. The Aungst et al article teaches that DMP 323 is to be used as an HIV protease inhibitor, and teaches that its solid dispersions improve the oral bioavailability of the active component, but does not actually teach administering the solid dispersion to a mammal in need thereof. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the solid dispersions of the Aungst et al article to a mammal in need of treatment of an HIV infection, because the Aungst et al article's solid dispersions would have been expected to effective in delivering a useful amount of an HIV protease inhibitor to a mammal in need of such treatment, and because it is prima facie obvious to administer drugs for their intended purpose.

7. Claims 1-5, 9, 11-13, 17, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by the Aungst et al article (B.T. Gattetosse, Vol. 87, pages 49-54). The Aungst et al article teaches a solid dispersion of DMP 323, an HIV protease inhibitor, in PEG. The solid dispersion can optionally comprise a surfactant. The solid dispersion is formed by solvent evaporation using a 50% ethanol:50% methylene chloride solvent. The solid dispersion is encapsulated in a hard gelatin capsule. See, e.g., the paragraph bridging pages 49 and 50 and Table 2.

8. Claims 10 and 14 are rejected under 35 U.S.C. 103(a) as being obvious over the Aungst et al article ((B.T. Gattetosse, Vol. 87, pages 49-54) as applied against claims 1-5, 9, 11-13, 17, and 18 above, and further in view of the WO Patent Application '499. The Aungst et al article teaches encapsulating its solid dispersions rather than formulating them into tablets. The WO Patent Application '499 teaches forming a solid dispersion of a drug having low water solubility in polyethylene glycol and adding a hydrophillic gel-forming polymer. The solid dispersions may be compressed into tablets for oral administration. See, e.g., the Abstract; page 7, lines 25-27; page 8, lines 16-20; and claims 1 and 12. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to formulate the solid dispersions of the Aungst et al article into tablets because the WO Patent Application '499 suggests the desirability of this pharmaceutical form for solid dispersions in which extended-release of the drug is desired.

9. Claim 19 is rejected under 35 U.S.C. 103(a) as being obvious over the Aungst et al article (B.T. Gattetosse, Vol. 87, pages 49-54). Application of the Aungst et al article is the same as in the above rejection of claims 1-5, 9, 11-13, 17, and 18. The Aungst et al article teaches that DMP 323 is to be used as an HIV protease inhibitor, and teaches that its solid dispersions

improve the oral bioavailability of the active component, but does not actually teach administering the solid dispersion to a mammal in need thereof. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the solid dispersions of the Aungst et al article to a mammal in need of treatment of an HIV infection, because the Aungst et al article's solid dispersions would have been expected to effective in delivering a useful amount of an HIV protease inhibitor to a mammal in need of such treatment, and because it is prima facie obvious to administer drugs for their intended purpose.

10. Claims 1-6, 9, 11, 19, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Al-Razzak et al (U.S. Patent No. 5,610,193). Al-Razzak et al teach a solid dispersion comprising compound III, i.e. ritonavir, in polyethylene glycol. See column 3, lines 29-33. With respect to instant claims 3 and 4, note that method of making steps do not impart patentability to product claims which are otherwise anticipated by or obvious over the prior art. Al-Razzak et al also teach a mixture of a pharmaceutically acceptable organic solvent (such as polyethylene glycol or preferably propylene glycol, both of which are water-soluble), an HIV protease inhibitor (which is preferably ritonavir), and an organic acid adsorbed onto a pharmaceutically acceptable adsorbent, optionally encapsulated in a hard gelatin capsule and optionally combined with a surfactant or an antioxidant. The compositions are administered to inhibit HIV infection and to treat AIDS in humans. See, e.g., column 3, lines 1-21; column 3, line 60 - column 4, line 48; column 4, line 56 - column 5, line 5; column 6, lines 19-32; column 29, lines 50-63; and claim 3. Note that the pharmaceutically acceptable adsorbent required by the compositions of Al-Razzak et al is permitted by the "comprising" language used by Applicants to define their claimed compositions.

11. Claims 12, 13, 15, 17, and 18 are rejected under 35 U.S.C. 103(a) as being obvious over Al-Razzak et al (U.S. Patent No. 5,610,193). Application of Al-Razzak et al is the same as in the above rejection of claims 1-6, 9, 11, 19, and 20. Al-Razzak et al teach combining an ethanol cosolvent with the organic solvent, e.g., the polyethylene glycol or propylene glycol, and then adding the HIV protease inhibitor (see column 9, lines 42-51), rather than first combining the ethanol cosolvent with the HIV protease inhibitor and then adding the mixture to the organic solvent as required by Applicants' claims. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to combine the components of Al-Razzak et al in the order claimed by Applicants because a slight change in the sequence of adding ingredients does not have any effect on the resulting mixture and is prima facie obvious. See MPEP 2144.04(IV)(C).

12. Claims 5-8, 15, 16, 20, and 21 are rejected under 35 U.S.C. 103(a) as being obvious over Al-Razzak et al (U.S. Patent No. 5,610,193) as applied against claims 1-6, 9, 11, 19, and 20 above or as applied against claims 12, 13, 15, 17, and 18 above, and further in view of Sham et al. Al-Razzak et al disclose including an HIV protease inhibitor generically, but do not teach a combination of ritonavir and ABT-378. Sham et al teach the desirability of administering combinations of ritonavir and ABT-378. See, e.g., column 79, lines 50-63, and column 82, lines 1-19 and 35-41. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer a combination of ritonavir and ABT-378 in the compositions of Al-Razzak et al because the compositions of Al-Razzak et al are applicable to HIV protease inhibitors generically and would permit the oral administration of Sham et al's active agents, because Sham et al disclose the desirability of administering combinations of

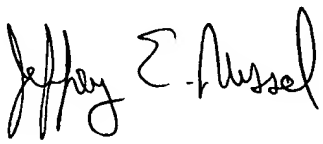
ritonavir and ABT-378, and because in the HIV treatment art it is desirable to administer multiple active agents so as to prevent the development of resistant virus strains.

13. Claims 1-6, 10, 19, and 20 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application '499 in view of the Aungst et al article (B.T. Gattetosse, Vol. 87, pages 49-54) or Al-Razzak et al (U.S. Patent No. 5,610,193). The WO Patent Application '499 teaches forming a solid dispersion of a drug having low water solubility in polyethylene glycol and adding a hydrophillic gel-forming polymer. The solid dispersions may be compressed into tablets for oral administration. See, e.g., the Abstract; page 7, lines 25-27; page 8, lines 16-20; and claims 1 and 12. The WO Patent Application '499 does not teach an HIV protease inhibitor as the drug. The Aungst et al article teaches DMP 323 to be a drug having low water solubility which it is desirable to form into an oral dosage form. See, e.g., page 49, column 1, first paragraph. Al-Razzak et al teach ritonavir to be a drug having low water solubility which it is desirable to form into an oral dosage form. See, e.g., column 3, lines 1-28, and column 29, lines 43-64. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the drugs of the Aungst et al article or Al-Razzak et al using the forms taught by the WO Patent Application '499 because the drugs taught by the Aungst et al article and by Al-Razzak et al are the same type of water-insoluble drugs with which the WO Patent Application '499 is concerned, and because the WO Patent Application '499 provides a pharmaceutical form which permits the oral administration of the drugs of the Aungst et al article and Al-Razzak et al. With respect to instant claims 3 and 4, note that method of making steps do not impart patentability to product claims which are otherwise anticipated by or obvious over the prior art.

14. The Aungst et al article (Int. J. Pharmaceutics, Vol. 156, pages 79-88) discloses a composition comprising DMP 323 in a mixture of Gelucire 44/14 and PEG 400. However, the disclosure of this composition is not relied upon to reject Applicants' claims, because Applicants' claims require a solid dispersion, whereas the Aungst et al article describe this composition as a semi-solid. See page 82, paragraph bridging columns 1 and 2, of the Aungst et al article.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Christopher Low can be reached at (703) 308-2923. The fax number for Art Unit 1653 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1653

JRussel

February 19, 2002